

AMENDMENTS TO THE CLAIMS

1. (currently amended) A high throughput method of identifying a function of a polypeptide-encoding ~~[[gene]]~~ sequence of interest endogenously expressed by ~~[[in]]~~ a cell type comprising:

a) ~~overexpressing all or part of said sequence in a first population of said cell type; providing at least a first and a second pseudotyped lentiviral vector, each comprising a least a part of the polypeptide-encoding sequence of interest or a complementary sequence thereof, wherein the first lentiviral vector is designed to overexpress the endogenously expressed polypeptide-encoding sequence of interest and the second lentiviral vector is designed to inhibit or terminate expression of the endogenously expressed sequence of interest, and both the first and the second pseudotyped lentiviral vector can only express the at least part of the polypeptide-encoding sequence of interest or complementary sequence thereof;~~

b) ~~inhibiting expression of said sequence in a second population of said cell type; providing a first and a second population of the cell type, and transducing the first lentiviral vector in the first cell population and transducing the second lentiviral vector in the second cell population;~~

c) ~~overexpressing all or part of said polypeptide-encoding sequence in the first population of said cell type and inhibiting or terminating expression of said polypeptide-encoding sequence in the second population of said cell type;~~

d) ~~[[e)]]~~ high throughput detecting at least one change ~~changes~~ in one or more endogenous cellular factors in said first and second populations and comparing the effect on the cell of overexpression of the polypeptide-encoding sequence with the effect on the cell of inhibition or termination of expression of the polypeptide-encoding sequence; and

e) ~~[[d)]]~~ identifying a ~~[[said]]~~ function of said polypeptide-encoding ~~[[gene]]~~ sequence of interest based on the detected and compared ~~identity of, or effect on the cell of overexpression and inhibition or termination of expression of~~ ~~[[;]]~~ said one or more cellular factors.

2. (currently amended) The method of claim 1 wherein said at least one change is an increase ~~changes are increases~~ and/or decrease ~~decreases~~ in the expression of said endogenous cellular factors.

3. (currently amended) The method of claim 1 wherein said at least one change is ~~changes are in a~~ ~~[[the]]~~ post-translational modification ~~modifications~~ of said endogenous cellular factors.

4. (currently amended) The method of claim 3 wherein said post-translational modification comprises a ~~changes are in the~~ phosphorylation or glycosylation of said cellular factors.

5. (currently amended) The method of claim 1 wherein said at least one change is ~~changes are in an~~ ~~[[the]]~~ activity of said cellular factors.

6. (currently amended) The method of claim 1 wherein said pseudotyped lentiviral vector ~~overexpressing of said gene sequence in a first population is by use of a~~ conditionally replicating pseudotyped lentiviral vector ~~that expresses said gene sequence.~~

7. (currently amended) The method of claim 1 wherein said inhibiting expression of said polypeptide-encoding ~~[[gene]]~~ sequence in a second population is by use of a pseudotyped lentiviral vector capable of expressing all or part of said polypeptide-encoding ~~[[gene]]~~ sequence in an antisense orientation.

8. (currently amended) The method of claim 1 wherein said inhibiting or terminating expression of said polypeptide-encoding ~~[[gene]]~~ sequence in a second population is by use of a pseudotyped lentiviral vector capable of expressing one or more ribozymes against said polypeptide-encoding ~~[[gene]]~~ sequence.

9. (currently amended) The method of claim 1 wherein said inhibiting or terminating expression of said polypeptide-encoding ~~[[gene]]~~ sequence in a second population is by the generation of post-transcriptional gene silencing (PTGS) against said polypeptide-encoding ~~[[gene]]~~ sequence.

10. (original) The method of claim 1 wherein said cell type is a primary cell.

Claims 11 to 13 (canceled)

14. (currently amended) The method of claim 1 wherein said polypeptide-encoding ~~[[gene]]~~ sequence of interest encodes a product which modulates expression of said one or more cellular factors by binding to nucleic acids encoding, or regulating the expression of, said one or more cellular factors.

15. (currently amended) The method of claim 12 wherein said polypeptide-encoding ~~[[gene]]~~ sequence of interest encodes a transcriptional activator.

16. (currently amended) The method of claim 12 wherein said polypeptide-encoding ~~[[gene]]~~ sequence of interest encodes a transcriptional repressor.

17. (currently amended) The method of claim 1 wherein said polypeptide-encoding ~~[[gene]]~~ sequence of interest is a human sequence.

18. (currently amended) The method of claim 1 wherein said cell type is a human, a plant or a microorganism cell type.

19. (previously presented) A method of altering the expression of one or more cellular factors in a cell comprising overexpressing or inhibiting the expression of a gene sequence for which a function was identified by the method of claim 1.

20. (previously presented) A method of altering the phenotype of a cell comprising overexpressing or inhibiting the expression of a gene sequence for which a function was identified by the method of claim 1.

21. (currently amended) A high throughput method of identifying a function of a gene sequence of interest in a cell heterologous to the cellular source of said gene sequence comprising:

a) providing at least a first and a second pseudotyped lentiviral vector, each comprising a least a part of the gene sequence of interest or a complementary sequence thereof,

wherein the first lentiviral vector is designed to overexpress the expressed gene sequence of interest and the second lentiviral vector is designed to underexpress or terminate the expressed sequence of interest, and overexpression and underexpression or termination is relative to the level

of expression of the gene sequence in the cell from which the gene sequence was derived, and both the first and the second pseudotyped lentiviral vector can only express the at least part of the gene sequence of interest or complementary sequence thereof;

(b) providing a first and a second population of the cell, and transducing the first lentiviral vector in a first cell population and transducing the second lentiviral vector in a second cell population;

(c) overexpressing all or part of said gene sequence in the [[a]] first population of said cell type; and b) inhibiting or terminating expression of said sequence in a second population of said cell type;

(d) e) high throughput detecting at least one change changes in one or more cellular factors in said first and second populations and comparing the effect on the cell of overexpression of the gene sequence with the effect on the cell of inhibition or termination of expression of the gene sequence; and

(e) d) identifying a [[said]] function of said gene sequence of interest based on the detected and compared identity of, or effect on the cell of overexpression and inhibition or termination of expression of [[;]] said one or more cellular factors.

22. (currently amended) A method of detecting a change in one or more cellular factors in a cell due to the overexpression or inhibition of a gene sequence of interest in said cell, comprising:

a) providing at least a first and a second pseudotyped lentiviral vector, each comprising a least a part of the gene sequence of interest or a complementary sequence thereof,

wherein the first lentiviral vector is designed to overexpress the expressed gene sequence of interest and the second lentiviral vector is designed to underexpress or terminate the expressed sequence of interest, and overexpression and underexpression or termination is relative to the level of expression of the gene sequence in the cell from which the gene sequence was derived, and both the first and the second pseudotyped lentiviral vector can only express the at least part of the gene sequence of interest or complementary sequence thereof;

(b) providing a first and a second population of the cell, and transducing the first lentiviral vector in a first cell population and transducing the second lentiviral vector in a second cell population;

(c) overexpressing all or part of said gene sequence in the [[a]] first population of said cell type [[i]] and b) inhibiting expression of said gene sequence in a second population of said cell type;
and

(d) e) high throughput detecting at least one [[a]] change in one or more cellular factors in said first and second populations by comparing the effect on the cell of overexpression of the gene sequence with the effect on the cell of inhibition or termination of expression of the gene sequence.

23. (currently amended) The method of claim 22, further comprising a step:

(e) d) identifying the function of said gene sequence of interest based on the detected and compared identity of, or effect on the cell of overexpression and inhibition or termination of expression of [[i]] said one or more cellular factors.

24. (currently amended) The method of claim 23, further comprising a step:

(f) e) altering the expression of said one or more cellular factors in a third population of said cell type cell by overexpressing or inhibiting the expression of said gene of interest for which a function was identified in step (e) d).

25. (currently amended) The method of claim 23, further comprising a step:

(f) e) altering the phenotype of a third population of said cell type by overexpressing or inhibiting the expression of said gene sequence of interest for which a function was identified in step (e) d).

26. (currently amended) The method of claim 22, wherein said cell is heterologous to the cellular source of said gene sequence of interest, and overexpression and underexpression or terminate is relative to the level of expression of the gene sequence in the cell from which the gene sequence was derived.

27. (currently amended) The method of claim 22, wherein said cellular factor comprises ~~[[is]]~~ a cellular gene product or a metabolite.

28. (currently amended) The method of claim 27, wherein said cellular gene product comprises ~~[[is]]~~ a protein or RNA.

29. (currently amended) The method of claim 27, wherein said metabolite comprises ~~[[is]]~~ a sugar or a lipid.

30. (new) The method of claim 1, wherein inhibiting or terminating expression of the polypeptide-encoding sequence is mediated by post-transcriptional gene silencing (PTGS), small interfering RNA (siRNA), RNA interference, or an antisense or a ribozyme sequence targeted against the polypeptide-encoding sequence.

31. (new) The method of claim 1, wherein the high throughput detecting comprises use of computerized or robot implemented systems.

32. (new) The method of claim 31, wherein the high throughput detecting comprises use of libraries of lentiviral vectors and cells transduced by the lentiviral vectors.

33. (new) The method of claim 32, wherein the high throughput detecting comprises use of libraries of lentiviral vectors and cells transduced by the lentiviral vectors in a multiplicity of compartments.

34. (new) The method of claim 1, wherein the high throughput detecting comprises use of machine implemented microarray or macroarray technology.

35. (new) The method of claim 21, wherein inhibiting or terminating expression of the gene sequence is mediated by post-transcriptional gene silencing (PTGS), small interfering RNA (siRNA), RNA interference, or an antisense or a ribozyme sequence targeted against the polypeptide-encoding sequence.

36. (new) The method of claim 21, wherein the high throughput detecting comprises use of computerized or robot implemented systems.